It can be seen on pages 2-3 of the Restriction Requirement dated 12 March 2002 that the claims of the invention in Groups I-VI all belong to the same classification (Class 424, subclass 93.71 and Class 435, subclass 372).

Furthermore, Applicants respectfully submit that consideration of the claims of Group I with the claims in Groups II-VI would not place a serious burden on the Examiner because the claims in Groups I-VI do not have a separate classification in the art, do not have a separate status in the art, and do not require a different field of search (see MPEP § 808.02).

Pending claims in Groups I-VI are all directed to compositions comprising "dendritic cell precursors." For instance, independent claim 82 is directed to an *in vitro* composition comprising an enriched and expanded population of proliferating dendritic cell precursors. Similarly, independent claim 96 is directed to a pharmaceutical composition comprising a therapeutic amount of an enriched and expanded population of proliferating dendritic cell precursors and a pharmaceutically acceptable carrier. Likewise, independent claim 101 is directed to an *in vitro* composition comprising a population of antigen-activated dendritic cell precursors, wherein said antigen-activated dendritic cell precursors present processed antigen derived from an enriched and expanded population of proliferating dendritic cell precursors, which were contacted *in vitro,* in the presence of GM-CSF, with antigen for sufficient time for said proliferating dendritic cell precursors to process and present said antigen. Thus, the Restriction Requirement is not proper.

Moreover, a search of the prior art for the composition comprising dendritic cell precursors of Group I, would necessarily encompass a search of the prior art for the compositions

comprising dendritic cell precursors in Groups II-VI. Thus, the prior art for Group I will also be the same prior art for Groups II-VI.

The Examiner opines that the Group I-VI inventions are drawn to "different products," and asserts that

> [i]nventions II-VI comprise different kinds of dendritic cells that [sic] would process and present antigen in different ways in different MHC contexts. For example, the dendritic cells of Invention IV would be considered Th1 dendritic cells, likely processing and presenting antigen in an MHC Class I context whereas the dendritic cells of Invention V would be considered Th2 dendritic cells, likely processing and presenting antigen in an MHC Class II context. Therefore the inventions are patentably distinct (03/12/02 Restriction Requirement, page 3).

Respectfully, there are not "different kinds of dendritic cells," as the Examiner contends. In particular, "Th1 dendritic cells" and "Th2 dendritic cells" do not exist. The terms "Th1" and "Th2" refer to subsets of CD4+ T helper cells and not dendritic cells.

While, it is possible for dendritic cell precursors to present antigen on MHC class I and/or MHC class II molecules for presentation to CD8+ and/or CD4+ T cells, respectively (see specification, *e.g.,* at page 6), the dendritic cell precursors according to the present invention only present the processed antigens on MHC class II molecules.

The enriched and expanded population of dendritic cell precursors according to the invention of claim 101 are contacted *in vitro* with antigen, and the cells internalize the particle by endocytosis or phagocytosis. For instance, the Applicants state on page 36 of the specification that

> [t]o the extent that endocytosis is required for antigen processing and presentation, it was not previously evident how dendritic cells would present particle-associated peptides. Based on out work, it is now evident that progenitors to dendritic cells which this invention provides can internalize such particles for

> processing and presentation. The types of particles which may be internalized by phagocytosis include bacteria, viral, mycobacteria or other infectious agents capable of causing disease. Accordingly, any antigenic particle which is internalized and processed by the dendritic cell precursors of this invention is also suitable for making the various immunogens, toleragens and vaccines as described as part of this invention. (lines 1-13).

As is well known by skilled artisans, when exogenous antigen—irrespective of the type—is contacted *in vitro* with the dendritic cells precursors, the antigen will be processed by the endocytic processing pathway for presentation on MHC class II molecules of the dendritic cell precursors. While it is possible that if *e.g.,* live virus is contacted with the enriched and expanded population of dendritic cell precursors *in vitro*, the precursors will be infected with virus and will, thus, present viral antigen on both MHC class I and class II molecules. However, this invention only involves the internalization of exogenous antigens, which are internalized by phagocytosis or endocytosis or both. Thus, these claims are not distinct and have not acquired a separate status in the art.

Accordingly, Applicants request reconsideration and withdrawal of the Restriction of Groups I-VI.

Applicants provisionally elect the claims of Group V (claims 84, 89, 91-92, 94-95, 97, 99, 101, and 103), with traverse, for prosecution at this time.

Applicants are submitting this Response within one month of the Restriction Requirement mailed 12 March 2002. Thus, no additional fees are due with this filing. However, please charge any underpayments or credit any overpayments to our Deposit Account No. 08-0219.

If there are any questions, please call the undersigned at the telephone number indicated below.

Date: 12 April 2002

HALE AND DORR LLP
1455 Pennsylvania Ave., NW
Washington, DC 20004
Tel: (202) 942-8332
Fax: (202) 942-8484

Tamera M. Pertmer, Ph.D.
Agent for Applicant
Reg. No.: 47,856

APPENDIX A

Pending Claims 82, 84-103

82. An *in vitro* composition comprising an enriched and expanded population of proliferating dendritic cell precursors.

84. The composition of dendritic cell precursors according to either one of claims 82 or 101, wherein the dendritic cell precursors are human.

85. The composition of dendritic cell precursors according to claim 84, wherein the dendritic cell precursors are obtained from blood.

86. The composition of dendritic cell precursors according to claim 84 wherein the dendritic cell precursors are obtained from bone marrow.

87. The composition according to claim 83 wherein the antigen is produced by tumor cells.

88. The composition according to claim 83 wherein the antigen is an immunoglobulin.

89. The composition according to claim 101, wherein the antigen is a microorganism.

90. The composition according to claim 83 wherein the antigen is a virus.

91. The composition according to claim 83 wherein the antigen is a polypeptide.

92. The composition according to claim 83 wherein the antigen is a peptide.

93. The composition according to claim 83 wherein the antigen is a self-protein or auto-antigen.

94. The composition according to claim 101, wherein the antigen is a mycobacteria tuberculosis bacteria.

95. The composition according to claim 94, wherein the mycobacteria tuberculosis bacteria is BCG.

96. A pharmaceutical composition comprising a therapeutic amount of an enriched and expanded population of human proliferating dendritic cell precursors and a pharmaceutically acceptable carrier.

97. The composition according to claim 96, wherein the dendritic cells are antigen-activated.

98. A mixed culture of activated dendritic cells and T cells.

99. The pharmaceutical composition according to claim 97, wherein the antigen-activated dendritic cells express an amount of modified antigen to provide between about 1 to 100 micrograms of modified antigen in said pharmaceutical composition.

100. A pharmaceutical composition comprising a dendritic cell modified antigen wherein a substance to be modified is exposed to a culture of isolated dendritic cell precursors and whereby the substance is modified by the dendritic cells to produce modified antigen.

101. An *in vitro* composition comprising a population of antigen-activated dendritic cell precursors, wherein said antigen-activated dendritic cell precursors present processed antigen derived from an enriched and expanded population of proliferating dendritic cell precursors,

which were contacted *in vitro,* in the presence of GM-CSF, with antigen for sufficient time for said proliferating dendritic cell precursors to process and present said antigen.

102. The composition of proliferating dendritic cell precursors according to claim 82 further comprising GM-CSF.

103. The pharmaceutical composition according to claim 97, wherein the pharmaceutical composition comprises from about $1x10^6$ to $1x10^7$ antigen-activated dendritic cell precursors.